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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,221	SANBERG ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *90,94,95 and 124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *90,94,95 and 124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 6, 2006 has been entered. Claims 90 and 94 have been amended. Claims 87, 89, 93, and 96-98 have been cancelled. Claim 124 has been newly added.

Accordingly, Claims 90, 94, 95, and 124 remain pending.

The amendment to the specification filed March 17, 2006 has been entered (see pages 2-3 of the amendment).

The remarks filed on March 17, 2006 (hereinafter referred to as "the response") and June 6, 2006 are considered herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 90, 94, 95, and 124 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims and newly added claims include new matter.

MPEP 2163.03 provides that an amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed. *In re Wright*, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989). Applicants should specifically point out the support for any amendments

made to the claims. MPEP 2163 states that new or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) and *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972).

The claims are directed to a method of producing an isolated, differentiated, mononuclear cell from human umbilical cord blood. Newly added Claim 124 recites "growing the mononuclear cells in a serum-free medium consisting of EGF, bFGF, pokeweed mitogen, Ara-C or a combination thereof to produce an enriched fraction of progenitor cells." However, the instant specification does not contemplate a serum-free medium consisting of these four components. The indefiniteness issue arising from the use of the closed claim language term "consisting of" is dealt with in the rejection under 35 U.S.C. 112, second paragraph, as set forth hereinbelow. However, even if the claim were amended to recite the open term "comprising", the new matter issue would remain because the as-filed specification clearly does not contemplate a serum-free medium comprising all four of these components. The specification only contemplates a serum-free medium comprising EGF and bFGF. At page 46, lines 9-13, under "General Methods", the specification describes serum-free "Neural Proliferation Medium" comprising, among other things, EGF and bFGF. There is no description of a serum-free medium that comprises EGF, bFGF, pokeweed mitogen, and Ara-C. Applicants have not pointed to any support in the as-filed specification for the newly added claim limitation. The Examiner has reviewed the specification and finds no support in the as-filed specification for such a culture medium. Thus, the as-filed specification does not contemplate or describe the culture medium as presently recited in the claims.

Thus, the amended claims and newly added claims include new matter.

Enablement

Claim 90 stands rejected and Claim 124 is rejected under 35 U.S.C. 112, first paragraph, for reasons of record, because the specification, while being enabling for

a method of producing an isolated, differentiated, mononuclear cell from human umbilical cord blood, comprising (a) obtaining a cord blood fraction comprising mononuclear cells from said umbilical cord blood, wherein the mononuclear cells comprise progenitor cells; (b) growing the mononuclear cells in a serum-free medium comprising EGF and bFGF to produce an enriched fraction of progenitor cells; and (c) culturing the enriched fraction of progenitor cells in a culture medium containing an effective amount of **retinoic acid and NGF** for a period sufficient to differentiate the progenitor cell to a cell of interest,

does not reasonably provide enablement for the use of other differentiation agents or other combinations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of enablement has been modified to more closely match the present claim language which now recites 3 steps instead of 2 steps.

The claims are directed to methods of producing neural cell compositions.

The specification fails to provide an enabling disclosure for the methods of making neural cell compositions because the specification teaches that the only use for the compositions produced is for therapeutic transplantation, but methods of transplantation of neural tissue or other cells into the CNS or PNS are not routinely successful and the specification does not offer adequate guidance to enable one skilled in the art to practice the claimed invention to derive a therapeutic benefit in a diseased animal. The specification teaches that the only use for the compositions produced from the claimed method is for transplantation to produce a therapeutic effect but the specification does not adequately teach how to use the cell compositions produced by the claimed method to produce such an effect. Jackowski et al. (1995)

details the limitations and unpredictability associated with the transplantation of neural tissue. At page 311, column 1, paragraph 2, the reference discusses the barriers to successful transplantation of neural tissue, notably the presence of molecules that actively inhibit the regeneration of mammalian CNS and PNS axons. Grados-Munro et al. (2003) further disclose that axon outgrowth inhibition is a major barrier to axon regeneration in the CNS. Various myelin-associated inhibitors have been identified and their *in vivo* inhibitory effects have been characterized. The authors contemplate that a combination of approaches, including treatment to neutralize the inhibitory character of the CNS environment, may be required for CNS regenerative therapy (page 479). Other problems relating to appropriate environmental cues for axon guidance are also discussed. Filbin (2003) also discloses that inhibitors of axonal regeneration are present in the adult mammalian CNS and further discusses the inhibitory effect of glial scars which form after injury. Growth cone collapse is noted as the first event in inhibition of axonal growth and the response of neurons to inhibitors is discussed, including the current state of the art with regard to the intracellular inhibitory signalling pathway. Mehler et al. (1999) details the unpredictability and technical problems encountered in using progenitor cells for neural regeneration, particularly in the CNS. The authors state that "the reconstitution of more complex and widespread neural populations damaged by a variety of genetic or acquired neurological disorders such as stroke or traumatic injury will require access to a broader array of neural lineage species and a greater understanding of the developmental signals that sanction integration into the host environments. Many studies have suggested that the normal adult brain may lack the appropriate environmental signals to allow neural progenitor species present in multiple mature CNS regions to realize their broad lineage potential" (page 781, column 2, paragraph 2). The instant specification does not offer specific guidance as to how the full scope of the compositions produced by the claimed method could be used therapeutically for the treatment of any disorder, including Parkinson's disease (PD), Alzheimer's disease (AD), Huntington's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Tay Sach's disease, Rett Syndrome,

lysosomal storage disease, ischemia, spinal cord damage, ataxia, schizophrenia, or autism, as contemplated in the specification. While the specification discloses the use of human cord blood fractions that have been used either directly upon thawing (cord blood mononuclear cells) or treated in culture for a week with various trophic factors (BDNF, NGF, EGF+bFGF) prior to transplantation into a rat stroke model (pages 58-65), the claims cover the preparation of a great variety of cell compositions, including terminally-differentiated cells, which the specification does not teach how to use. The human cord blood fractions used directly upon thawing are not the cells produced by the claimed methods, but rather appear to be the starting material for use in the claimed method. **With regard to the cells that were cultured with various trophic factors, the specification does not disclose the phenotype of these cells and the claims require the production of cells that exhibit an increase in the expression of genes associated with neurogenesis.** The example at page 58 of the specification states that "[a]nimals which received the retinoic acid+NGF treated mononuclear cells were able to stay on a rotating axle longer and fell off fewer times in the 3 minute test period than did all other animals in the study." This statement is relied upon for the scope of enablement indicated hereinabove. However, nothing further is disclosed about the treatment of cord blood mononuclear cells with retinoic acid+NGF. The disclosure provides no specifics in terms of the length of time the cells were cultured in the presence of the factors, the amount of each factor, or other parameters of the culture conditions. Nothing is disclosed in terms of the "increase in expression of genes associated with neurogenesis and a decrease in the expression of genes associated with hematopoiesis" as recited in the claim. Thus, it is unclear that culture in the presence of retinoic acid+NGF meets the present claim limitations relating to the gene expression profile of the "cell of interest." Other than the stroke example presented at page 58, the specification provides general teachings only (see pages 1-8 of specification), but does not provide specific guidance for treating a pathological condition, using cell compositions over the full scope of the claims. The specification fails

to provide specific guidance for using the great variety of cell compositions covered by the claims, to provide a therapeutic benefit for the treatment of a disease or disorder.

As a further issue, it is noted that the claims now recite "culturing the progenitor cells in a culture medium" in step (c). Thus, the claims now read on culturing purified progenitor cells, when only an enriched fraction of progenitor cells is obtained in the preceding step. However, for the reasons noted below in the full enablement rejection of Claims 94 and 95, the instant specification does not teach any method for obtaining purified progenitor cells. The specification provides no guidance with regard to purifying the progenitor cell of interest from the cord blood mononuclear cells. This aspect of the rejection could be overcome by reciting "culturing the enriched fraction of progenitor cells," as noted in the scope of enablement indicated above.

Given the limited applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the wide variety of cell types and cell compositions that could be produced using the claimed methods, and the unpredictability for using the cell compositions produced to achieve a therapeutic effect upon transplantation as asserted in the specification, one of skill in the art would have been required to engage in undue experimentation to practice the claimed methods to make cell compositions that meet the claim limitations and further to use the cell compositions produced by the claimed methods.

At page 6, paragraph 3 of the response, Applicants note that the present claim language is broader than the scope of Claim 87, but Applicants offer no arguments regarding enablement for this broader scope. The claims currently cover using retinoic acid in combination with either NGF, BDNF, or GDNF to effect differentiation, but this is broader than the indicated scope of enablement and no arguments are offered as to why the combinations of retinoic acid with either BDNF or GDNF would be considered enabled. The specification only provides specific guidance with regard to the combination of retinoic acid with NGF (see the example at page 58 of the specification and Table I). The example at page 58

notes that cells treated with BDNF or NGF were used in the transplantation experiments, but only cells treated with retinoic acid and NGF produced a beneficial result in the transplant experiments. The specification states "[a]nimals which received the retinoic acid + NGF treated mononuclear cells were able to stay on a rotating axle longer and fell off fewer times in the 3 minute test period than did all other animals in the study" (page 58, lines 10-12). As noted in the rejection of record, this statement is relied upon for the scope of enablement indicated hereinabove (page 5, paragraph 1 of the Office Action mailed 10/20/05).

At page 6, paragraph 4 of the response, Applicants note that the specification describes the use of retinoic acid with NGF, BDNF, and GDNF at page 46, lines 13-15. While the specification **contemplates** using a differentiation medium containing retinoic acid in combination with NGF, BDNF, or GDNF, there is no teaching of achieving the claim-designated result with either BDNF or GDNF, and Applicants offer no arguments with regard to the **enablement** of these other embodiments.

At page 6, paragraph 5 of the response, Applicants argue that the rat MCAO model was used to test transplantation of the neural compositions produced by the claimed method and that rotarod scores were significantly improved with NGF+RA HUCB treatment. Applicants are reminded that the Examiner has already indicated that claims of this scope are enabled. Applicants provide no arguments or evidence with regard to enablement for the other embodiments (i.e., RA+BDNF and RA+GDNF treated cells).

At page 7, paragraph 2 of the response, Applicants assert that Jackowski discloses that "CNS implants in adult brains survive" and that "NGF receptors are also widely present and play a significant role in mammalian CNS development, particularly in the case of cholinergic neurons." Applicants conclude that Jackowski's comments support implanting early stage neuron-like cells treated with NGF, such as the cells prepared by the claimed method. While not agreeing with Applicants conclusion, as Jackowki does not discuss successfully implanting early stage neuron-like cells (whether treated with NGF or not), Applicants are again reminded that the Examiner has already indicated a scope of

enablement for cells treated with retinoic acid and NGF. No arguments have been presented with regard to enablement for the other embodiments (i.e., RA+BDNF and RA+GDNF treated cells).

At pages 7-8 of the response, Applicants acknowledge that Grados-Munro et al. (2003) teaches that axon outgrowth inhibition is a major barrier to axon regeneration in the CNS and that the authors contemplate that a combination of approaches, including treatment to neutralize the inhibitory character of the CNS environment, may be required for CNS regenerative therapy. Applicants assert that since the inventive cells are derived from young umbilical cells, it is pertinent that Grados-Munro mentions that young mice show substantial corticospinal sprouting proximal to a spinal cord dorsal hemisection in a number of corticospinal axons below the lesion (p. 481). However, those mice underwent no transplantation at all and therefore cannot be said to demonstrate that transplantation of progenitor cells is therapeutic. The regeneration that was observed was regeneration by endogenous cells. No transplant was performed. Furthermore, Grados-Munro et al. (2003) is post-filing art and therefore is not representative of what was known in the art at the time of filing. The priority date of this application is March 2000.

At page 8, paragraph 2 of the response, Applicants acknowledge that Filbin discloses inhibitors of axonal regeneration. Applicants assert that Filbin states that "New molecular information has also accumulated on how the neuron can be changed intrinsically to overcome myelin inhibitors." However, since Filbin (2003) is post-filing art, the teachings of Filbin cannot be relied upon to supply that which is missing from the instant application. One of skill in the art would not have had the benefit of the "new molecular information" that Filbin refers to at the time the invention was made. The priority date of this application is March 2000.

At page 8, paragraph 3 of the response, Applicants dismiss the teachings of Mehler because the instant application teaches that young cells differentiated from HUCB cells according to the invention have been found to correct neurological deficits. However, only mononuclear cells differentiated with

retinoic acid and NGF were found to correct neurological deficits. This scope has already been acknowledged as being enabled. There is no evidence that mononuclear cells treated with other neurotrophic factors could correct neurological deficits. On the contrary, the specification discloses that such experiments **were performed** and only cells treated with retinoic acid and NGF were capable of improving a neurological deficit (see the specification at page 58).

At page 9, paragraph 1 of the response, Applicants dispute the Examiner's assertion at page 5 of the prior Office Action (mailed 10/20/05) that "nothing further is disclosed about the treatment of cord blood mononuclear cells with retinoic acid+NGF." Applicants go on to cite the teachings of the specification under the General Methods section. However, the statement was made with regard to the transplantation experiment described at page 58. Applicants cite the teachings for various studies described throughout the specification, but not for the particular transplantation experiment described at page 58, that was cited for demonstrating the therapeutic result. For example, Applicants refer to page 28 of the specification for teaching that cells were cultured in DMEM for 10 days. However, the experiments described at page 28 pertain to generating **clones** from cord blood cells. The claimed invention does not pertain to or involve the generation of clones from cord blood cells.

At page 9, paragraph 2 of the response, Applicants assert that Table I teaches increased expression of markers indicative of neurogenesis in cells treated with RA+NGF. The Examiner accepts the teachings of Table I as pertaining to mononuclear cells treated with RA+NGF. Applicants are again reminded that a scope of enablement for cells treated with RA+NGF has already been acknowledged. Applicants further assert that Table II teaches that there was a decrease in the expression of genes associated with hematopoiesis and that it can be inferred that "the cells of interest in Table II were treated with at least the RA+NGF method." No support is offered for this assertion. Applicants are reminded that Attorney argument cannot take the place of actual evidence. See MPEP § 2145 and 716.01(c)(II).

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze* 145 USPQ 716, 718 (CCPA 1965).

At page 10, paragraph 3 of the response, Applicants assert that the limited trophic factors now claimed were used to process the cells used in the animal model and to achieve significantly beneficial results. It appears that the animal model and beneficial results Applicants are referring to pertain to the MCAO model used in the transplantation experiment described on page 58. Contrary to Applicants' assertion, a beneficial result was only achieved when cells treated with NGF+RA were used for transplantation. Also contrary to Applicants' assertion, cells treated with **GDNF** were **not** used in the animal model.

Applicants have not offered any arguments directed to the non-enabled scope, i.e. cells treated with retinoic acid and either **BDNF** or **GDNF**.

The references cited in the rejection of record support the contention that therapeutic transplantation into the mammalian CNS is unpredictable and that different cell types produce very different results, with no clear guidance on which cell types or differentiation methods will work to provide a therapeutic outcome upon transplantation of those cells. Intensive effort has been applied by the research community in attempting to identify and produce cell compositions that are effective in treating a variety of CNS diseases, with limited success. The result of this intensive effort is that the art as a whole teaches that methods of identifying and producing cell compositions that are capable of producing a therapeutic effect are unpredictable.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

Claims 94 and 95 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 94 and 95 are directed to the aforementioned method of producing an isolated, differentiated mononuclear cell from human umbilical cord blood, wherein the progenitor cells are isolated from the mononuclear cells using a magnetic cell separator to separate out cells expressing a particular CD marker.

The reasoning set forth above in the scope of enablement rejection applies equally to Claims 94 and 95. In addition, there is no scope of enablement for these claims for the following reasons. The claims require isolation of the progenitor cells from the mononuclear cells, but the specification fails to provide an enabling disclosure for separating the progenitor cells from the mononuclear cells.

The specification provides no guidance with regard to isolating the progenitor cell of interest from the cord blood mononuclear cells. The specification contemplates that the progenitor cell of interest may be a mesenchymal stem cell present in cord blood that has the capability to differentiate into neural cells and that it may therefore be a CD34-negative cell. However, the specification provides no fractionation methods beyond separating whole cord blood to obtain mononuclear cells and separating cord blood cells to obtain CD34-negative cells (page 27). The specification does not identify the cell type that is responsible for producing the neural cells appearing after differentiation. At pages 27-28 of the specification, the disclosure teaches how to obtain cord blood cells that are negative for CD34. However, this cell fraction is not further used in experiments to determine if it retains the progenitor cell that is responsible for producing the differentiated neural cells. The art demonstrates the difficulty of identifying a desired progenitor or stem cell from a heterogeneous population of cells and the further difficulty of purifying or isolating that stem or progenitor cell from the heterogeneous cell population (Bonnet, 2002). For example, Bonnet discusses the difficulties encountered in identifying and separating distinct subpopulations of CD34+ cells to obtain hematopoietic stem cells with long-term repopulating capability.

Although, hematopoietic stem cells have been studied for many years, the author discloses that "[t]he elucidation of the molecular phenotype of the HSC has just begun" (abstract).

Given the limited applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to separation methods that may be used to isolate the progenitor cells from the mononuclear cells, and the unpredictability for using the cell compositions produced to achieve a therapeutic effect upon transplantation as asserted in the specification, one of skill in the art would have been required to engage in undue experimentation to practice the claimed methods to make cell compositions that meet the claim limitations and further to use the cell compositions produced by the claimed methods.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

No arguments have been offered in response to this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 90, 94, and 95 stand rejected and Claim 124 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 90, 94, and 95 remain indefinite and Claim 124 is indefinite in their recitation of "increase" and "decrease" because it is unclear what would be considered the reference state for said "increase" or said "decrease". The claims now recite that the cell of interest should be compared to an "umbilical cord blood cell that has not been cultured in the presence of the differentiation agent" but the term "umbilical cord blood cell" covers a variety of different cell types, given that "umbilical cord blood" refers to a heterogeneous population of cells. Thus, it is unclear which cell type should be used as the reference cell. Is it the progenitor cell itself (i.e., the cell that gives rise to the cell of interest)? In the

absence of recitation of some reference state or process for comparison said "increase" and said "decrease" remain indefinite. Since "umbilical cord blood" refers to a heterogeneous population of cells it remains unclear which cell type should be used as the reference cell.

At page 10 of the response, Applicants assert that page 38 of the specification states "total RNA obtained from human cord blood cells, with or without RA+NGF treatment, from different batches were pooled together for this experiment ..." Applicants conclude that the **specification** delineates that the reference state is untreated HUCB (without RA+NGF treatment), whereas the test sample is RA+NGF-treated cord blood cells. Applicants are arguing limitations that are not in the claims. The Office cannot read limitations from the specification into the claims. The **claims** recite "in comparison to an umbilical cord blood cell that has not been cultured in the presence of the differentiation agent." This reads on using an untreated red blood cell as the reference state because an untreated red blood cell is indeed "an umbilical cord blood cell that has not been cultured in the presence of the differentiation agent." As the claim reads now, the reference cell can be **any** umbilical cord blood cell.

Claims 90, 94, 95, and 124 are indefinite in their recitation of "a serum-free medium consisting of EGF, bFGF, pokeweed mitogen, Ara-C or a combination thereof" because use of the closed claim language "consisting of" is wholly inconsistent with the elements recited thereafter. Clearly, a serum-free medium cannot "consist of" EGF alone or even all four elements alone. Such a medium would include no water, no glucose, nor any of the other essential elements of a culture medium. That's not a culture medium. As further issue, use of the closed claim language "consisting of" is inconsistent with the use of the term "or" because the term "consisting of" denotes required and defined elements, whereas the term "or" denotes optional elements.

Claims 90, 94, 95, and 124 are indefinite in their recitation of "selected from the group of BDNF, NGF, and GDNF" because it is unclear if this claim language is intended to be open claim language or

closed claim language. Amendment to recite "selected from the group consisting of BDNF, NGF, and GDNF" would be remedial.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER